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10/040,206	01/02/2002	Vishwanath R. Lingappa	UCSF.002.01US	1150

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EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,206	LINGAPPA ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-14 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-14, 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 16, 2005 has been entered.

Claims 12-14, 51-54 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Priority

Priority was discussed in the Office action of July 2, 2003. To reiterate claims making reference to the knock out mouse or the sequence of the HP68 kD protein will only be granted priority to the filing date of the instant application January 2, 2002.

Claim Rejections - 35 USC § 112

The rejection of claims 12-14 and 51-54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is maintained** essentially for reasons of record.

Argument: Applicants urges that the specification supports the existence of at least two tertiary structures of the amino acid sequence set out in SEQ ID NO:6. The supposed existence of two tertiary structures is based on an immunoprecipitation experiment (Figure 14 in the

specification) in which Applicants find that HP68 associates with Gag when Gag is expressed in Cos-1 cells. Applicants point to this experiment as indicating that there are two different conformers (i.e. two different conformational structures of the same protein; structure A and structure B) where one conformation structure associates with Gag and another conformational structure associates with RNase L inhibitor.

Response to argument: From the experimental design this is not the only interpretation that can explain the results. The results can also be interpreted as follows: (1) the HP68 may have a higher affinity for Gag and therefore the cellular pool of HP68 will associated with Gag when Gag is present in the cell and thereby no longer associate with RNase L, or (2) alternatively the presence of a plasmid or Gag in the cell may stimulate the cell to produce more of the RNase L inhibitor which then binds to RNase L displacing HP68 form the RNase L. Either scenario does not support that there are structural differences between HP68 when it associates with Gag or RNase L [see Martinand et al. RNase L inhibitor is induced during human immunodeficiency virus type 1 infection and down regulates the 2-5A?RNase L pathway in human T cells. Journal of Virology (Jan. 1999) Vol. 73, No. 1, pages 290-296; or Bisbal et al. Cloning and characterization of RNase L inhibitor. Journal of Biological Chemistry (1995) Vol. 270, No. 22, pages 13308-13317]. The experiement set out in Figure 14 does not provide evidence that there actually are two different conformational structures of the same protein. Even if there are actually two different conformational structures of the same protein Applicants have not provided a means of distinguishing one structure from the other. Thus the ordinary artisan would not know how to tell the structures apart.

Argument: Applicants additionally make the argument that the scenarios posed by the Examiner are inept because the data generated by the Applicants uses a cell free system, therefore no cellular pool of HP68 is present. Applicants' argument on this point is not convincing.

Response to argument: The sole thrust to convince the Office that there are two different conformational structures of the same protein is based on the experiments set out in Figure 14. The experiments of Figure 14 utilize a cell transfection assay using Cos-1 cells (Cos-1 cells are eukaryotic cells and therefore by definition the experiments are not based on a cell free system). Figure 14 does not provide evidence that there are two different conformational structures associated with HSP68. The experiment uses an immunoprecipitation procedure in which a polyclonal antibody against HuHP68 was used to precipitate the HP68 complexes. Cells transfected with plasmid carrying Gag or BruΔenv were subjected to immunoprecipitation. The result that only Gag was precipitated with HP68 was interpreted by Applicant's to mean that there are two conformational structures "conformers" for HP68. Here Gag could simply have higher affinity for HP68 without HP68 having a different structure.

Argument: Applicants argue that the term conformer is well known in the art and that the use of antibodies is an accepted method of distinguishing between different conformers. Additionally, Applicants point to the specification for a definition of conformer (specification page 8, lines 26-28).

Response to argument: Applicant makes reference to two exhibits (Exhibit A and Exhibit B), please note that these exhibits are not present in the file. The exhibits appear to be

references, these references have not been presented on a 1449 form and are not found in the file thus the references have not been evaluated.

The reference of Irnatan et al. appears to be making reference to a gastric sodium potassium ATPase pump. In this case antibodies were made to distinguish between the E1 and E2 conformational structure. Here, the only way the ordinary artisan would know the difference between the E1 and E2 structure is to actually use the antibodies from the reference. Injecting an animal with the SDS denatured sodium potassium ATPase pump revealed that large stretches of the gastric sodium potassium ATPase pump were not antigenic at all. That a protein can take on two different conformational shapes depending on the sodium or potassium concentration in the solution was previously described using the fluorescein (FITC) quenching model. Thus the art indicates that structural differences in gastric sodium potassium ATPase pump were previously known. The different conformational shapes could be stabilized depending on the sodium or potassium concentration in the solution, thus antibodies could be screened against either structural conformer. In the instant case there is a question whether HP68 actually forms two different structural conformations. Even if it forms the two different structures there is no evidence that structures can be stabilized to a point that antibodies can be screened to preferentially bind one structure. Thus the Office does not doubt that antibodies can be used to distinguish between two different structures. The problem is that you actually need to be in possession of such an antibody to determine the different structures. Thus you need an antibody so that you can define the structure, which then allows you to compare the ability of other antibodies to bind the same structure. In this case the specification does not have a written description of the necessary antibody.

The definition in the specification does not help describe the conformer because the specification indicates that a conformer can be more than just a different conformational structure a conformer can include different amino acid sequences. "...protein having at least substantially the same amino acid sequence, but heterogeneity in structure." That definition allows proteins conformer structures that is close (substantially similar does not equal the same or identical) in amino acid sequence but is not identical. This definition broadens the meaning of the term conformer and does not help further define the structure.

The term "conformer" renders the claims indefinite because the ordinary artisan would not know what is meant by this term. The specification has not provided a way to distinguish between the "conformers" (i.e. two different conformational structures of the same protein). The phrase "conformer" renders the claims indefinite because the specification does not provide a standard of ascertaining the conformation the term is indefinite. The specification has not provided a way to distinguish between the "conformers." See MPEP § 2173.05(f).

The rejection of claims 12-14 and 51- 54 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention **is maintained** for reason of record.

Argument: Applicant argues that there may well be many different interpretations of their data, but for purpose of the instant prosecution it is Applicants interpretation of the data that controls.

Response to argument: Applicants specification is not reviewed in a vacuum. The specification is reviewed with what is generally known in the art, and the experimental results in the specification are interpreted accordingly. Using sound scientific reasoning after reviewing the specification Applicants data does not show that the HP68 protein actually forms two separate and distinct structures, HP68 structure A and HP68 structure B.

Argument: Applicant argues that it is well settled that difficult and time consuming is not the same as "undue experimentation."

Response to argument: In this instance the rejection is made because Applicants have not provided a written description for the knock-out animals that are to be used for the production of the antibodies. A generic description of how to hopefully achieve the production of a knock-out animal is not sufficient. In this instance if the animal does not survive to a sufficient age to actually produce antibodies, the antibodies can simply never be made using the claimed process.

Applicants have not provided a description of the actual structure, by describing the actual epitopes to which these antibodies bind. Thus without more the ordinary artisan could not envision the two different conformer structures claimed, let alone antibodies that bind to only one of the conformers.

Argument: Applicants' argument is that the rejected "claims are original claims in the application as filed, and therefore, by definition applicants were in possession of the claimed subject matter at the time the application was filed."

Response to argument: Applicants' arguments are not convincing, applicant is advised to review the written description guidelines that became effective in January 5, 2001. (64 FR 71427, Dec 21, 1999 and in the Official Gazette at 1231 O.G. 123, Feb. 29, 2000). The

guidelines require that "[t]he analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicants has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art." Knock-out mice and the production of such mice is not a trivial matter and that the general description would not be sufficient to describe the particular mouse needed for the invention. Merely adding method steps to the claim does not provide a description of the animal.

There is insufficient written description for the claimed antibodies that require the existence of a knock-out mouse. The knock-out mouse is not described in the specification and there are no antibodies disclosed that were made using such a knock out mouse. The claims encompass a genus of compounds (monoclonal antibodies) defined only by their function "binding to a conformer" without disclosing the structural differences between the "conformers." There is no objective evidence in the specification as filed that would indicate the binding affinity differences in the HP68 molecule is due to conformational constraints of the HP68 molecule itself. Even if there are actual conformational differences there is no evidence that would indicate Applicants were in possession of an antibody or any other means of detecting the difference in the structure.

The specification has not provided a written description of how to determine the difference in structure between the "the conformation of the chaperone protein involved in the assembly of immature viral particles and the conformation of the chaperone that do not bind

Gag." The claims remain rejected because the specification does not provide sufficient written description for the knock-out mouse and the antibodies produced using such a knock-out mouse.

Neither the specification nor the prior art has provided any teaching regarding an HP68 knock-out animal, i.e. a mouse with a homozygous disruption of the gene encoding HP68. The specification has not disclosed any monoclonal antibodies produced by the methods as claimed. All transgenic models, whether targeted or untargeted, still present unpredictable expression patterns due to incomplete knockout of the targeted gene, redundancy within the genome or unanticipated genetic interactions, such as down-regulation of other genes. (Taconic Newsletter, March 1996, Vol. 1, No. 2, page 4).

The claims encompass a genus of compounds (monoclonal antibodies) defined only by their function "binding to a conformer" without disclosing the structural differences between the "conformers." Applicant makes reference to figure 14 as evidencing that there are two different conformational structures that are associated with HSP68. The experiment uses an immunoprecipitation procedure in which a polyclonal antibody against HuHP68 was used to precipitate the HP68 complexes. Cells transfected with plasmid carrying Gag or BruΔenv were subjected to immunoprecipitation. The result that only Gag was precipitated HP68 was interpreted by Applicant's to mean that there are two conformational structures "conformers" for HP68. This interpretation is not convincing because (1) the HP68 may have a higher affinity for Gag and therefore the cellular pool of HP68 will associated with Gag when present in the cell, (2) or alternatively that the presence of a plasmid or Gag in the cell may stimulate the cell to produce the RNase L inhibitor which then binds to RNase L displacing HP68 form the RNase L. Either scenario does not indicate that there are actual structural differences between HP68 when

it associates with Gag or RNase L [see Martinand et al. RNase L inhibitor is induced during human immunodeficiency virus type 1 infection and down regulates the 2-5A?RNase L pathway in human T cells. Journal of Virology (Jan. 1999) Vol. 73, No. 1, pages 290-296; or Bisbal et al. Cloning and characterization of RNase L inhibitor. Journal of Biological Chemistry (1995) Vol. 270, No. 22, pages 13308-13317]. The fact that one could have assayed/screened for a compound of interest does not overcome this defect since one would have no knowledge beforehand as to whether or not any given compound would fall within the scope of what is claimed. In order to measure binding to a particular conformation structure would require that this tertiary structure is stable.

The claimed invention is drawn to an antibody identified by the method of claim 12. However, no structural or specific functional characteristics (specific epitope binding) of such an antibody is provided, nor is there any indication that the artisan actually implemented the method of claim 12 so as to identify any monoclonal antibodies. This situation is analogous to that of *Regents of the University of California v Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention.* The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.) Because one skilled in the art would conclude that the inventors were not in possession of the claimed invention. The claim fails to comply with the written description requirement.

The instant invention is drawn to a method of making monoclonal antibodies, these antibodies are to the chaperone protein involved in the capsid assembly but the antibodies do not bind the conformer that does not bind Gag. The specification has disclosed the production of polyclonal antibodies to wheat germ derived and human derived C-terminal HP68 peptide sequences. The method (claim 12) requires the use of a knockout mouse to produce antibodies. Neither the specification nor the prior art has provided any teaching regarding such a knockout animal. The specification also has not disclosed any monoclonal antibodies derived by the method.

Creating new, genetically engineered animal research models involves two transgenic techniques. (1) the classical pronuclear microinjection: introduction of foreign DNA into embryonic pronuclei resulting in random integration and (2) expression and embryonic stem (ES) cell-mediated gene targeting: introduction of genetically modified ES cells into recipient embryos resulting in the ablation (knockout) or modification of a specific genetic expression (Taconic Newsletter, March 1996, Vol. 1, No. 2, page 4). All transgenic models, whether targeted or untargeted, still present unpredictable expression patterns due to incomplete knockout of the targeted gene, redundancy within the genome or unanticipated genetic interactions, such as down-regulation of other genes (Taconic Newsletter, March 1996, Vol. 1, No. 2, page 4). Thus without actually making the knock-out animal the ordinary artisan could not predict that the animal will survive long enough to actually be able to produce antibodies.

To comply with the written description requirement of 35 U.S.C. § 112, first paragraph, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An

applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was ready for patenting" such as by the use of drawings or structural chemical formulas that show that the invention was complete, or describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

The rejection of claims 12-14, 51-54 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention **is maintained** for reasons of record.

Argument: Applicants arguments are that they have avoided this rejection by amending the claims to set out specific steps used to produce the knock out mouse.

Response to argument: The amendment and the arguments fail to address the unpredictability in the art of making knockout animals. The rejection is maintained for reason of record.

The specification has not provided a means to distinguish the difference in structure between the "the conformation of the chaperone protein involved in the assembly of immature viral particles and the conformation of the chaperone that do not bind Gag." Applicants' specification hypothesizes that there are different structural conformation of the same protein. The hypothesis is based on the different binding affinities of the HP68 and the different targets.

The different binding affinities between the different targets could just as well be based on the structure of the target and have nothing to do with the structure of the HP68. Yet the claims are broadly drawn to include methods of distinguishing different structures of HP68 when it has not been established that HP68 even has different structures. Because the creation of a knock-out mouse is unpredictable, the creation of antibodies using this animal will also be unpredictable.

Argument: Applicant's arguments are that the methods of making a knock-out mouse are well established in the art and that the structure of the monoclonal antibody is not important *per se* but rather the three dimensional structure of the protein "conformer" used to generate the monoclonal antibody is significant.

Response to argument: Neither the specification nor the prior art has provided any teaching regarding a HP68 knockout animal. The specification also has not disclosed any monoclonal antibodies produced by the claimed method. All transgenic models, whether targeted or untargeted, still present unpredictable expression patterns due to incomplete knockout of the targeted gene, redundancy within the genome or unanticipated genetic interactions, such as down-regulation of other genes (Taconic Newsletter, March 1996, Vol. 1, No. 2, page 4). Indicating that until an animal has actually been created there is uncertainty. The claims as written do not appear to require germline transmission of the disrupted nucleotide sequence. It would be unpredictable if a disruption of a nucleotide sequence in a single cell would result in a phenotype (that would not have any HP68 protein in the animal). The instant specification has not provided any uses for a transgenic mouse that does not exhibit a phenotype resulting from disruption of a nucleotide sequence (see below). The claims encompasses transgenic mice that comprise a disruption in a host chaperone protein encoding gene, particularly the nucleotide

sequence of HP68. Claims 12 embrace transgenic mice exhibiting a particular phenotype, wherein a broad interpretation of the claimed animals could read on disruption of a host chaperone protein encoding gene in a single cell. The specification has not taught that transgenic mouse embryos whose genomes comprise a homozygous disruption of the HP68 encoding gene and that these animals do not exhibit a phenotype of embryonic lethality. The state of the art at the time the invention was filed was such that one of skill could not predict the phenotype of a knockout mouse [Moreadith et al. Gene targeting in embryonic stem cells: the new physiology and metabolism. Journal of Molecular Medicine (1997) Vol. 75, pages 208-216; see page 208, column 2, last full paragraph]. Another example of unpredictability was the inactivation of the gene encoding cytokine receptor chain in transgenic mice resulted in a phenotype different from that expected [Leonard et al. Role of the common cytokine receptor gamma chain in cytokine signaling and lymphoid development. Immunological Reviews. (1995) No. 148, pages 97-114]. Finally, Moens et al. (Defects in heart and lung development in compound heterozygotes for two different targeted mutations at the N-myc locus. Development (1993) Vol. 119, pages 485-499) disclose that two mutations produced by homologous recombination in two different locations of the N-myc gene produce two different phenotypes in mouse embryonic stem cells, one leaky and one null (see abstract). It would be difficult to predict any phenotype resulting from disruption of the sequence encoding HP68 in light of the above. Moreover, as the claims read on disruption of a host chaperone protein (HP68) protein encoding gene in a single cell, it would be unpredictable if such a disruption would result in any phenotype. The specification has not disclosed a transgenic mouse embryos whose genome comprises a homozygous disruption in the nucleotide sequence encoding the HP68 gene does not display embryonic lethality. Given the

unpredictable nature of a phenotype that results from disruption of a nucleotide sequence it would required undue experimentation for the skilled artisan to make and use the invention as claimed.

The claims encompass a genus of compounds (monoclonal antibodies) defined only by their function "binding to a conformer" without disclosing the structural differences between the "conformers." Applicant makes reference to figure 14 as evidencing that there are two different conformational structures that are associated with HSP68. The experiment uses an immunoprecipitation procedure in which a polyclonal antibody against HUHP68 was used to precipitate the HP68 complexes. Cells transfected with plasmid carrying Gag or BruΔenv were subjected to immunoprecipitation. The result that only Gag was precipitated HP68 was interpreted by Applicant's to mean that there are two conformational structures "conformers" for HP68. This interpretation is not convincing because (1) the HP68 may have a higher affinity for Gag and therefore the cellular pool of HP68 will associated with Gag when present in the cell, (2) or alternatively that the presence of a plasmid or Gag in the cell may stimulate the cell to produce the RNase L Inhibitor which then binds to RNase L which will then displace HP68 form the RNase L. Either scenario does not indicate that there are structural differences between HP68 when it associates tithe Gag or RNase L [see Martinand et al. RNase L inhibitor is induced during human immunodeficiency virus type 1 infection and down regulates the 2-5A?RNase L pathway in human T cells. Journal of Virology (Jan. 1999) Vol. 73, No. 1, pages 290-296; or Bisbal et al. Cloning and characterization of RNase L inhibitor. Journal of Biological Chemistry (1995) Vol. 270, No. 22, pages 13308-13317].

Making antibodies to a conformational structure is not a trivial matter and requires more than a mere road map on how applicants envision the production of this antibody. The generic procedure of immunizing a homozygous knockout animal with a protein having a stable conformational structure does not predictably result in the production of antibodies that can recognize/distinguish one conformer over the other conformer [see Prusiner et al. Ablation of the prion protein (PrP) gene in mice prevents scrapie and facilitates production of anti-PtP antibodies. Proceeding of the National Academy of Science (1993) Vol. 90, pages 10608-10612]. The lack of PrP^{C} in PrP-p0/0 mice prevents them from becoming tolerant to the immunogen, the injection of the PrP^{Sc} infectious structure into the animal produced antibodies against both PrP structures **but these antibodies did not distinguish between the prion conformers**. "Surprisingly, given that we immunized mice with infectious Prp27-30 preparation, none of the rescued antibodies exclusively recognized this form of protein, whereas all but one antibody reacted well with a PrP^{C} as it occurs on the cell surface" [see Williamson et al. Mapping the prion protein using recombinant antibodies. Journal of Virology (1998) Vol. 72, No. 11, pages 9413-9418, page 9417, column 1, 2nd paragraph].

The fact that one could have assayed/screened for a compound of interest using the claimed methods does not overcome this defect since one would have no knowledge beforehand as to whether or not any given compound would fall within the scope of what is claimed. In order to measure binding to a particular conformation structure it would require that this tertiary structure is stable. It would require undue experimentation (be an undue burden) to randomly screen undefined compounds for the claimed activity. The instant fact pattern fails to disclose that a monoclonal antibody has been produced using the claimed knock-out animal. The

specification does not provide any guidance or any working examples in this unpredictable art, and thus the artisan would have been unable to have prepared the claimed antibody without undue experimentation. Furthermore an assay for finding a product is not equivalent to a positive recitation of how to make such a product. This claim fails to meet the enablement requirement for the "how to make" prong of 35 U.S.C. § 112 first paragraph.

Claim Rejections - 35 USC § 102

The rejection of claim 13 under 35 U.S.C. 102(b) as being anticipated by Willison et. al (Cell, 1989) as evidenced by applicants specification page 45 lines 25-27 indicating that the 23c antibody was used for the isolation of the WG68 conformer **is maintained** for reasons of record.

Argument: Applicant urges that the reference does not disclose that the 23c antibody binds to the conformational specific structure of the chaperone.

Response to argument: The antibody binding ability to bind an epitope is an inherent feature of the antibody. The reference discloses the 23c antibody, the same antibody that applicants used to identify the HP68 from capsid intermediate structures. According to the specification HP68 is immunoreactive with 23c antibody and HP68 performs similar function as WG68 in hosting HIV assembly (see specification example 9). Thus, the reference by disclosing the monoclonal 23c antibody anticipates the instant invention.

A product by process claim is interpreted as "a composition of matter." Product by process claims are not limited to the manipulations of the recited steps in the prior claims from which the instant claim is now dependent on, only to the structure implied by the steps. M.P.E.P. Section 2113 states that:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted)

The cited art discloses the monoclonal antibody that was used in the process of identifying a chaperone protein WG68 found in wheat germ extract. The 23c antibody also recognizes a number of eukaryotic proteins.

The instant invention is drawn to a monoclonal antibody that binds HP68. The recitation "conformational specificity for host chaperone protein that is involved in assembly of immature HIV capsid and not to conformers of said host chaperone protein that do not bind Gag and do not facilitate HIV capsid assembly" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Willison et al. discloses the production of a 23c hybridoma cell line producing a monoclonal anti-TCP-1 alpha antibody, now available for purchase form Stressgen Biotechnologies (see table 1). This antibody was used by Applicant's to isolate the WG68 from wheat germ extracts, indicating that a known antibody structure bind HP68. Therefore, the instant invention drawn to monoclonal antibodies is anticipated by Willison et al.

Claim Rejections - 35 USC § 103

The rejection of claims 13 and 14 under 35 U.S.C. 103(a) as being obvious over Willison et. al (Cell, 1989) is maintained for reasons of record. as evidenced by applicants specification page 45 lines 25-27 indicating that the 23c antibody was used for the isolation of the WG68 conformer **is maintained** for reasons of record.

Argument: Applicant urges that the reference does not disclose that the 23c antibody binds to the conformational specific structure of the chaperone.

Response to argument: The antibody binding ability to an epitope is an inherent feature of the antibody. The reference discloses the 23c antibody, the same antibody that applicants used to identify the HP68 from capsid intermediate structures. According to the specification HP68 is immunoreactive with 23c antibody and HP68 performs similar function as WG68 in hosting HIV assembly (see specification example 9). Thus the reference by disclosing the monoclonal 23c antibody anticipates the instant invention.

The cited art teaches the monoclonal antibody that was used in the process of identifying a chaperone protein found in wheat germ extract. The 23c antibody recognizes a number of eukaryotic proteins. Once an antibody is known and isolated, the binding fragments of the antibody are obvious. The rejection is maintained.

Conclusion

No claims allowed.

This is a Request for Continued Examination (RCE) of applicant's earlier Application No. 10/040206. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL**

even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PH.D
PRIMARY EXAMINER